EXHIBIT B

BIODEGRADABLE HYDROGELS FOR DRUG DELIVERY

Kinam Park
Waleed S. W. Shalaby
Haesun Park
Purdue University, School of Pharmacy

TECHNOMIC PUBLISHING CO., INC.
LANCASTER · BASEL

van der Waals forces and
mer chains is great, it may
lecular hydrogen bonding
,es of cellulose is so strong
ıg and after hydration, the
1/or the polymer backbone
yzed hydrolysis to result in
ed polymers, the polymer
ıer the polymer backbone,
of the polymer chains leads
ystems, the reduction in the
loss of coherence between
weight degradation products
rom the body [29].

polymers dissolve in water.
ylic acid), poly(styrene sul-
readily dissolve in water by
ter molecules. Other polar
oly(ethylene oxide) (PEO),
o readily dissolve in water by
es.

the hydrophilic polymer in
hydrogel [28]. This hydrogel
nposition [31]. Once a gel is
ough a rather loose network
on further addition of water,
ndividual polymer molecules
rally referred to as erosion or
rd the core and finally the gel
he dissolution rate of water-
molecular weight and stereo-

epends on the amount of water,
the concentration of polymer
concentration at which the gel
polymer. At a given polymer
l and vice versa by varying the
ure, pH, or type of salt.

2.2.2 Charge Formation Followed by Dissolution

2.2.2.1 IONIZATION OR PROTONATION

Some polymers are initially water-insoluble but become solubilized by ionization or protonation of a pendant group. Examples are shown here.

$$\text{R-COOH} + \text{OH}^- \rightleftharpoons \text{R-COO}^- + \text{H}_2\text{O}$$

$$\text{R-CH}_2\text{NR}_2 + \text{H}^+ \rightleftharpoons \text{R-CH}_2\overset{+}{\text{N}}\text{HR}_2$$

Insoluble **Highly soluble**

The solubility of polyacids is strongly pH-dependent. At low pH solution, polyacids are not water-soluble because the carboxyl groups of polyacids are protonated, i.e., not ionized. Upon an increase in the pH of the solution, the carboxyl groups release hydrogen atoms and become ionized. As the content of the ionized groups gradually increases, the polymer becomes more hydrophilic, absorbs water, swells, and finally dissolves in water. The solubility of polybases also strongly depends on pH, but the trend is opposite to that of polyacids. Polybases are water-soluble at low pH ranges.

Polyacids have been used widely as enteric coating materials for pharmaceuticals. They are poorly water-soluble in low pH environments, such as in the stomach, and dissolve in alkaline conditions such as those found in the intestines. The pH-sensitive polymers that have been used as enteric coating materials are shellac (esters of aleuritic acid), cellulose acetate phthalate, cellulose acetate succinate, polyvinyl acetate phthalate, hydroxypropylmethylcellulose phthalate, and poly(methacrylic acid-*co*-methyl methacrylate) [32]. Among these, the most widely used polymers for enteric coating are cellulose acetate phthalate, poly(vinyl acetate phthalate), and poly(methacrylic acid-*co*-methyl methacrylate) [33,34]. The structures of these enteric coating polymers are shown in Figure 2.1. Cellulose acetate phthalate becomes water-soluble at a pH greater than 6, while poly(vinyl acetate phthalate) and hydroxypropylmethylcellulose phthalate are ionized at a lower pH [35].